Application No.: 10/812,849 Docket No.: 31075/40037 Examiner: D. Kolker Art Unit 1649

Response to action of 12/21/07

## **Amendment to the Claims**

## 1-16. Canceled

17. (Currently amended) A method of delivering an active agent into the central nervous system of an animal comprising administering to said animal a conjugate comprising said agent conjugated to a <u>Receptor Associated Protein (RAP)</u> RAP polypeptide consisting of an amino acid sequence at least 80% identical to amino acids 221-323 of RAP (SEQ ID NO: 1), wherein said RAP polypeptide retains megalin-binding activity and wherein said agent is delivered into the central nervous system.

- 18. (Currently amended) A method of increasing transcytosis of an active agent across the blood-brain barrier of an animal, comprising administering to said animal a conjugate comprising said agent conjugated to a Receptor Associated Protein (RAP) RAP polypeptide consisting of an amino acid sequence at least 80% identical to amino acids 221-323 of RAP (SEQ ID NO: 1), wherein said RAP polypeptide retains megalin-binding activity and wherein said agent is transcytosed across the blood-brain barrier.
- 19. (Currently amended) A method of treating a disorder of the CNS in a mammal comprising administering to said mammal a conjugate comprising an effective amount of a therapeutic agent conjugated to a <u>Receptor Associated Protein (RAP)</u> RAP polypeptide consisting of an amino acid sequence at least 80% identical to amino acids 221-323 of RAP (SEO ID NO: 1).

## 20. Canceled

- 21. (Previously presented) The method of claim 19, wherein said disorder is selected from the group consisting of Huntington's Disease, Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, Amylotrophic Lateral Sclerosis, ischemia-related disease and stroke, spinal muscular atrophy, cerebellar degeneration, perivenous encephalitis, schizophrenia, epilepsy and a central nervous system cancer.
- 22. (Withdrawn) The method of claim 21, wherein said disorder is a central nervous system cancer and said agent is a cancer chemotherapeutic agent.

## 23-57. Canceled

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58. (Previously presented) The method of claim 17 or 18 wherein the animal is a human.

- 59. (Previously presented) The method of claim 58 wherein the human is suffering from a disorder selected from the group consisting of Huntington's Disease, Alzheimer's Disease, Parkinson's Disease, Multiple Sclerosis, Amylotrophic Lateral Sclerosis, ischemia-related disease and stroke, spinal muscular atrophy, cerebellar degeneration, perivenous encephalitis, schizophrenia, epilepsy and a central nervous system cancer.
- 60. (Previously presented) The method of claim 17 or 18 wherein the agent is a neurotrophic factor.
- 61. (Previously presented) The method of claim 17 or 18 wherein the therapeutic agent is a neurotrophic factor selected from the group consisting of Glial-Derived Neurotrophic Factor, Nerve Growth Factor, Brain-Derived Neurotrophic Factor, Neurotrophin-3, Neurotrophin-4/5, aFGF, bFGF, CNTF, Leukaemia Inhibitory Factor, Cardiotrophin-1, TGFb, BMPs, GDFs, Neurturin, Artemin, Persephin, EGF, TGFa, Neuregulins, IGF-1, IGF-2, ADNF and PDGF.
- 62. (Previously presented) The method of claim 17 or 18 wherein the therapeutic agent is brain-derived neurotrophic factor (BDNF).